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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/700,179	07/27/2001	Pantaleone Paul Masci	65064/133	2781

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EXAMINER	
CHISM, BILLY D	

ART UNIT	PAPER NUMBER
1654	

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DATE MAILED: 02/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/700,179	MASCI ET AL.	
	Examiner	Art Unit	
	B. Dell Chism	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *41-45,47 and 48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-40 and 46* is/are rejected.

7)☒ Claim(s) *4 and 8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/13/00; 04/16/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 1-40 and 46 in Paper filed 02 December 2003 is acknowledged. The traversal is on the ground(s) that the Willmott *et al.* reference did not teach a single stage competitive plasmin inhibitor preparation that was substantially pure. This is not found persuasive because Applicants' disclosure of "substantially pure" (page 20 lines 14-24) does not support the claim limitation or the argument posed by Applicants. The definition does not set limitations on the % purity. In fact, the specification only states "typically" what a "substantially pure" preparation would be, however, the term "typically" is not defined or supported by art.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

2. Claim 8 is objected to because of the following informalities: claim 8 recites the term "Ph" at page 68 line 26, wherein the term should be deleted and replaced with "Phe". Claim 8 is also objected to for the improper recitation of the term "of" in part (h) at page 69 line 23, wherein the word should read be deleted and replaced with "or". Appropriate correction is required.

3. Claim 4 is objected to because of the following informalities: claim 4 is missing the term "sec^{-1}" in the range values. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 8-40 and 46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for plasmin inhibitors of SEQ ID NOs: 2, 4, 6, 8, 10 and 12, only those variants thereof described by the general formula of claim 9, and only those plasmin inhibitors of SEQ ID NOs: 16, 18, 20, 22, 24 and 26 comprising the leader sequence of SEQ ID NO: 14, does not reasonably provide enablement for fragments of the plasmin inhibitors of SEQ ID NOs: 2, 4, 6, 8, 10 and 12, or variants/derivatives other than those defined in claims 9-38, or enablement for in vivo alleviation of blood loss. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of

experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention and breadth of the claims: The claimed invention is drawn to a plasmin inhibitor consisting of a sequence from the list consisting of SEQ ID NOs: 2, 4, 6, 8, 10, 12, 16, 18, 20, 22, 24 and 26, however, the breadth of the claims are to the above mentioned plasmin inhibitors and numerous fragments and variants/derivatives thereof, that are not disclosed in the general formula of claim 9, and the in vivo administration of any of the above mentioned compounds for the alleviation of blood loss.

The state of the prior art and the predictability or lack thereof in the art: The prior art lacks teachings regarding the claimed plasmin inhibitors with the fragments and variants/derivatives thereof other than the general formula of claim 9, especially for in vivo use to alleviate blood loss, thus, the predictability of said compounds/compositions is unpredictable.

Willmott *et al.* 1995 (Fibrinolysis, Vol. 9 pates 1-8, cited in previous office action) teaches a serine protease inhibitor from the Australian brown snake, however, there are no teachings regarding those presently claimed sequences, fragments and variants/derivatives thereof, especially for in vivo use to alleviate blood loss.

The amount of direction or guidance present and the presence or absence of working examples: Given the lack of teachings regarding the predictability of all fragments and variants/derivatives for the SEQ ID NOs: 2, 4, 6, 8, 10, 12, 16, 18, 20, 22, 24 and 26 and the use of said compounds for in vivo alleviation of blood loss, detailed teachings are required to be present in the disclosure to enable the skilled artisan to make and use all possible fragments and variants/derivatives for the SEQ ID NOs: 2, 4, 6, 8, 10, 12, 16, 18, 20, 22, 24 and 26, to use them for in vivo alleviation of blood loss. Such teachings are absent. There is no disclosure of all fragments and variants/derivatives for the SEQ ID NOs: 2, 4, 6, 8, 10, 12, 16, 18, 20, 22, 24 and 26, only the variants encompassed by the general formula of claim 9, there is also no disclosure for in vivo use to alleviate blood loss,.

The quantity of experimentation needed: Given the lack of teachings of predictability found in the art for all fragments and variants/derivatives for the SEQ ID NOs: 2, 4, 6, 8, 10, 12, 16, 18, 20, 22, 24 and 26 and for in vivo use to alleviate blood loss, and in the absence of sufficient disclosure in applicant's specification to overcome the lack of teachings of predictability, it would require undue experimentation by one of skill in the art to be able to make and use the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

7. Claims 1-40 and 46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected for the indefinite recitation of the phrase, "substantially pure" wherein the specification does not properly define the metes and bounds of the phrase, especially where Applicants' rely upon the phrase to distinguish the claimed invention from that known in the prior art.

Claims 2-40 and 46 are rejected for depending from rejected claim 1.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-40 and 46 are rejected under 35 U.S.C. 102(a) as being anticipated by Masci *et al.* 1999 (WO99/58569). The published international application is used in this rejection since the chain of priority is severed by change of inventorship. The inventorship of a national stage entry under 35 U.S.C. 371 is that inventorship set forth in the international application (37 CFR §1.41(a)(4). If the inventorship is changed in the national stage from that of the international stage, then Applicants must follow procedures of 37 CFR §1.497 (d)(1)-(4) wherein documentation is required to establish inventorship. As is, the priority of this national stage

entry is severed, thus, the international application, WO99/58569, is published prior art against the present application.

10. Claims 1 and 5-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Willmott *et al.* 1995 (cited above). Willmott *et al.* teach a preparation of a single stage competitive inhibitor of plasmin of claim 1 (see entire document, especially page 5) with a dissociation constant in the range of 10^{-7} M range that applies to those ranges in claims 5-6 (see page 6 right column).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to B. Dell Chism whose telephone number is 571-272-0962. The examiner can normally be reached on 7:30 AM - 4:30 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

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B. Dell Chism
03 February 2004

CHRISTOPHER R. TATE
PRIMARY EXAMINER